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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANGELL, JON E	
ART UNIT	PAPER NUMBER
1635	

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10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/916,017	DEBENEDETTI ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Action is in response to the communication filed on October 30, 2002, as Paper No.10. Claims 10, 11, 12 and 14-18 have been amended. New claims 19-27 have been added. Claims 1-27 are pending in the application. Claims 1-9 have been withdrawn from consideration as being drawn to a non-elected invention for the reasons of record. Claims 10-27 are examined herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 23, 25, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 23 recites the limitation "the vector of claim 21" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 25 depends on claim 23 and is rejected for the same reason. It is noted that claim 22 appears to be the only preceding claim drawn to a vector. Therefore, for examination purposes, claim 23 is interpreted as the vector of claim 22, rather than the vector of claim 21.

6. Claim 26 recites the limitation " the vector of claim 21" in line 2. There is insufficient antecedent basis for this limitation in the claim. It is noted that claim 22 appears to be the only preceding claim drawn to a vector. Therefore, for examination purposes, claim 26 is interpreted as a pharmaceutical composition comprising the vector of claim 22, rather than the vector of claim 21.

7. Claim 27 recites the limitation "the pharmaceutical composition of claim 25" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is noted that claim 26 appears to be the only preceding claim drawn to a pharmaceutical composition. Therefore, for examination purposes, claim 27 is interpreted as the pharmaceutical composition of claim 26, rather than the pharmaceutical composition of claim 25.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 10, 11, 13, 14 17, 18 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Shimogori et al. (BBRC Vol. 223:544-548; 1996).

Shimogori et al. teaches a DNA sequence comprising a promoter operably linked to a transcription sequence that when transcribed, produces a mRNA comprising a translatable sequence encoding the conditional toxin Thymidine Kinase (TK) and an untranslated sequence. Specifically, Shimogori teaches a vector that produces a mRNA comprising a 5' untranslated

region (UTR) linked to a translatable sequence encoding TK (a conditional toxin) wherein the 5'UTR comprises a 188 nucleotide GC-rich sequence of the 5'UTR of ornithine decarboxylase (ODC) (for e.g. see abstract; p. 545, last two paragraphs; and "Construction of plasmids" under Materials and Methods). The 188 nucleotide 5'UTR taught by Shimogori has a 56% GC-rich content, "thus this region can form a GC stem structure composed of three or more GC pairs." (See p. 545, under "Results and Discussion"). Therefore, the DNA taught by Shimogori comprises a 5'UTR having the elements necessary to inhibit translation of the toxin under conditions that exist within normal mammalian cells that do not express eIF4E and to allow translation of the toxin under condition that exist within mammalian cells that overexpress eIF4E relative to normal cells. Furthermore, the 5'UTR taught by Shimogori comprising a 56% GC-rich content which can form a GC stem structure composed of three or more GC pairs would inherently have a secondary structure conformation having a stability of $\Delta G \geq 50$Kcal/Mol.

Response to Arguments

10. Applicant's arguments filed 10/30/02 have been fully considered but they are not persuasive.

11. Applicants contend that the 5'UTR described does not contain each and every limitation required by the present claims. Applicants assert that the 188 bp sequence does not encompass the full 5'UTR of ODC, which was found to respond to the eIF4E level.

12. As mentioned above, the sequence of Shimogori comprises 188 bp of the ODC 5'UTR which is 56% GC-rich and able to form a GC stem structure composed of three or more GC pairs. It is noted that the prior art indicates that the 5'UTR of Spi-1 comprises a 151 bp GC-rich region that inhibits translation in cells with low levels eIF4E and allows translation in cells that

overexpress eIF4E (see van der Velden et al. 1999, cite in IDS, Table 1, p. 90). Therefore, the 188 bp sequence utilized by Shimogori is long enough, and comprises a high GC-rich content require to form secondary structures which would inherently inhibit translation when eIF4E concentration is low and allow translation when eIF4E levels are high. Therefore, the rejection of the claims under 35 USC 102 is appropriate, and the rejection is maintained.

Claim Rejections - 35 USC § 103

13. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 10, 11, 13, 14, 17, 18, 20, 21, 22, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koromilas et al. (EMBO 1992, cited in IDS) in view of Li B.D. et al. (Cancer 1997, cited in IDS) and further in view of Anderson L.M. et al. (Gene Therapy 1999, cited in IDS).

It is noted that claim 26 is interpreted as a pharmaceutical composition comprising the vector of claim 22, rather than the vector of claim 21, for the reasons mentioned in the 112 second paragraph rejection.

Koromilas teaches a DNA sequence which produces a mRNA comprising a 5'UTR linked to a reporter sequence which produces a reporter molecule when translated wherein the 5'UTR confers translational regulation of the reporter sequence such that the reporter sequence is not translated in cells which do not express eIF4E, but is translated in cells which overexpress eIF4E (e.g., see p. 4153, abstract; p.4155, Figure 3; and 4156, Figure 5). Koromilas also teaches that 5'UTRs which conferred said translational regulation required a theoretical standard free energy of about –50kcal/mol (see Fig. 3 and Fig. 5). Koromilas indicates that the DNA sequence described above can be cloned into a vector (specifically pSV2CAT), which can be used to produce said mRNA. Koromilas indicates that the plasmid can be precipitated in a solution of calcium phosphate (a pharmaceutically acceptable carrier), and then transfected into target cells (see p. 4157, under "Cell lines and DNA transfection") Specifically, Koromilas teaches that when the plasmid which produces said mRNA is transferred into test cells, constructs comprising a 5'UTR with a ΔG value = -32.7kcal/mol translated the reporter in all cells regardless of eIF4E concentration. However, constructs comprising a 5'UTR with a ΔG values = -57.7 and -81.7 kcal/mol translated the reporter only in all cells which overexpressed eIF4E. Indicating the any mRNA comprising a 5'UTR with a free energy ΔG value about –50kcal/mol linked to any translatable sequence would confer translational regulation of the translatable sequence as described.

Koromilas does not indicate that eIF4E is overexpressed in cancer cells, or that the translatable sequence that is linked to the 5'UTR is a toxin.

Li teaches that eIF4E is not significantly expressed in normal or benign breast specimens examined, but eIF4E is expressed in all breast carcinoma specimens examined (see, p. 2385, under "Results"; and p. 2386, Figure 1). Specifically, Li teaches that the ductal carcinoma specimens examined showed overexpression of eIF4E in the intermediate range (2.5-fold) while the breast carcinomas showed elevation in the 3-30-fold range.

Furthermore, Anderson teaches that herpes thymidine kinase (TK) is a "suicide gene" which can be used to kill a cell in which it is expressed. Specifically, Anderson teaches an adenoviral construct comprising a TK gene driven by a breast tissue-specific promoter (see p. 854, abstract). Anderson also teaches, "the therapeutic gene should be expressed in the cells of interest, while avoiding expression in non-target cell populations... transcriptional targeting of a heterologous gene using tissue/tumor specific promoters would theoretically provide an effective treatment regimen for both solid and metastatic tumors in vivo." (See p. 854, first two paragraphs).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the construct taught by Koromilas such that the reporter sequence is substituted with the sequence of TK (taught by Anderson) in order to translate the TK sequence specifically in breast carcinoma cells (which overexpress eIF4E, as taught by Li) with a reasonable expectation of success.

As mentioned above, Koromilas teaches that any mRNA comprising a 5'UTR with a free energy ΔG value about -50kcal/mol linked to any translatable sequence would confer

translational regulation of the translatable sequence, Li teaches that breast carcinoma cells (but not normal cells) overexpress eIF4E, and Anderson teaches that TK can be used to kill the cell that it is expressed in. Thus providing the motivation to one of ordinary skill in the art to make the described modifications in order to make a system for specifically expressing the TK gene specifically in breast cancer cells in order to kill the breast cancer cell and to prevent expression of the TK gene in non-cancerous cells.

16. Claims 10 and 12-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koromilas et al. (EMBO 1992, cited in IDS) in view of Li B.D. et al. (Cancer 1997, cited in IDS) and of Anderson L.M. et al. (Gene Therapy 1999, cited in IDS), and further in view of Willie (Int. Journ. Biochem. Cell Biol., 1999, cited in IDS).

Claims 10, 13, 14, 17 and 18 are rejected for the reasons set forth above in the 103 rejection. Additionally, claims 12, 15, 16 and 19 are rejected for the following reasons.

Koromilas, Li and Anderson taken together suggest a method for specifically expressing a gene of interest in a cell which overexpresses eIF4E (mentioned above). Briefly, the method suggested above comprises a DNA which expresses an mRNA comprising a 5'UTR is linked to a sequence of interest wherein the 5'UTR inhibits translation of the sequence of interest in cells that do not express eIF4e, and allows translation of the sequence of interest in cells which overexpress eIF4E. The 5'UTR could be any 5'UTR sequence with a ΔG value about –50 kcal/mol, the cells which overexpress eIF4E could be breast carcinoma cells, and the sequence of interest could be the herpes TK gene sequence. The DNA would be useful for expressing the

conditionally cytotoxic TK gene in breast cancer cells in order to specifically kill the cancer cell and not non-cancer cells.

Koromilas, Li and Anderson do not teach that the 5'UTR used to confer translational regulation to the mRNA is the 5'UTR of FGF-2 or the 5'UTR of the proto-oncogene c-myc.

Willis teaches, "There are numerous examples of highly structured 5'UTRs which inhibit the translation of the downstream cistron although the precise mechanisms are often unknown." (See p. 75, first column). Willis also teaches, "A group of mRNAs has been identified which includes those encoding c-myc, FGF-2 and PDGF which share up to four features [including]… (iii) they are translated in a cap-dependent manner and the translational repression of the 5'UTR is relieved in cells which overexpress eIF4E." (See paragraph bridging p. 79-80). Regarding the 5'UTR of c-myc, Willis indicates, "The 5'UTR does not inhibit the translation of downstream reporter genes or c-myc in HeLa cell extracts, or in HeLa, HepG2, or Cos-1 cells in vivo." (See p. 80, second column). Regarding the 5'UTR of FGF-2, Willis teaches, "Translational de-regulation of FGF-2 in breast carcinoma appears to occur by a cap-dependent mechanism since it has been shown that tumors which contain elevated levels of eIF4E also display increased levels of FGF-2…" (See p. 83, second paragraph). Willis also indicates that translational de-regulation of FGF-2 expression may cause FGF-2 overexpression in tumors such as breast, pancreatic and endometrial cancers (see paragraph bridging p. 82-83).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the construct taught by Koromilas such that the 5'UTR taught by Koromilas was substituted with the 5'UTR of c-myc or the 5'UTR of FGF-2 and such that the reporter sequence taught by Koromilas was substituted with the sequence of TK (taught

by Anderson) in order to translate the TK sequence specifically in HeLa, HepG2 or Cos-1 cells using the 5'UTR of c-myc; or alternatively to translate the TK sequence specifically in pancreatic or endothelial tumor cells using the 5'UTR of FGF-2, with a reasonable expectation of success.

As mentioned above, Koromilas teaches that any mRNA comprising a 5'UTR with a free energy ΔG value about −50kcal/mol linked to any translatable sequence would confer translational regulation of the translatable sequence, Li teaches that breast cancer cells (but not normal cells) overexpress eIF4E, Anderson teaches that TK can be used to kill the cell that it is expressed in, and Willis teaches that the 5'UTRs of c-myc and FGF-2 are translated in a cap-dependent manner such that the translational repression of the 5'UTR is relieved in cells which overexpress eIF4E including HeLa cells (c-myc 5'UTR) and pancreatic tumor cells (FGF-2 5'UTR). Thus providing the motivation to one of ordinary skill in the art to make the described modifications in order to make a DNA for expressing the TK gene in specific tumor cells such as HeLa cells (using the 5'UTR of c-myc) and pancreatic tumor cells (using the 5'UTR of FGF-2) in order to kill the tumor cells and to prevent expression of the TK gene in non-cancerous cells.

17. Claims 10, 22, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimogori et al. (BBRC Vol. 223:544-548; 1996) in view of De Benedetti et al. (Nucleic Acids Research, 1991; 8:1924-1931, cited in IDS).

It is noted that claim 23 is interpreted as the vector of claim 22, rather than the vector of claim 21, for the reasons mentioned in the 112 second paragraph rejection.

Claims 10 and 22 are rejected over Shimogori for the reasons set forth above in the 102 rejection.

However, Shimogori does not teach that the vector comprising the DNA sequence of claim 10 is a viral vector, or that the viral vector is a BK vector.

De Benedetti teaches a novel BK virus-based episomal vector for expression of foreign genes in mammalian cells. Specifically, De Benedetti teaches that the pBK shuttle vector is based on the SV40 and the human papova virus BK (see p. 1925, first column). De Benedetti also indicates that pBK is maintained in a episomal form in several human cell lines, resembling productive infection of the virus and pBK replicates at high copy number which can be varied by changing the G418 concentration in the culture medium (see p. 1925, first column).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the pBK shuttle vector taught by De Benedetti such that pBK comprised the DNA sequence taught by Shimogori, as mentioned above (claim 10), with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to make a pBK vector which is capable of expressing the DNA sequence taught by Shimogori in order to analyze the translational regulation of the GC-rich 5'UTR in cells as opposed to in vitro (as taught by Shimogori).

18. Claims 10, 22, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimogori et al. (BBRC Vol. 223:544-548; 1996) in view of GIBCO/BRL (1993-1994 catalog, p. 9-19 only).

It is noted that claim 27 is interpreted as the pharmaceutical composition of claim 26, and claim 26 is interpreted as the vector of claim 22, for the reasons mentioned in the 112 second paragraph rejection.

Claims 10 and 22 are rejected over Shimogori for the reasons set forth above in the 102 rejection.

However, Shimogori does not teach a pharmaceutically composition comprising the DNA sequence and a carrier such as a liposome complex carrier.

GIBCO/BRL (1993-1994 catalogue) teaches a liposome complex carrier, known as Lipofectin reagent (see p. 9-19) that is suitable for transfecting nucleic acids into tissue culture cells. Specifically, It is indicated that Lipofectin reagent comprises a cationic lipid (DOTMA) and a neutral lipid (DOPE) which forms a liposome complex with nucleic acids. The liposome-nucleic acid complex fuses with plasma membranes and transfers the nucleic acid into the cells.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to take the vector comprising the DNA sequence of claim 10 (taught by Shimogori) and combine it with the Lipofectin reagent (taught by GIBCO/BRL catalogue) in order to transfect the vector into cells in culture, with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to make a composition comprising the vector which is capable of expressing the DNA sequence (taught by Shimogori) and the liposome complex carrier (taught by GIBCO/BRL catalogue) in order to transfect the vector into cells where the translational regulation of the 5'UTR could be analyzed in a cell, rather than in vitro.

19. Claims 10, 22, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koromilas et al. (EMBO 1992, cited in IDS) in view of Li B.D. et al. (Cancer 1997, cited in IDS) and Anderson L.M. et al. (Gene Therapy 1999, cited in IDS), and further in view of De Benedetti et al. (Nucleic Acids Research, 1991; 8:1924-1931, cited in IDS).

It is noted that claim 23 is interpreted as the vector of claim 22, rather than the vector of claim 21, for the reasons mentioned in the 112 second paragraph rejection.

Claims 10 and 22 are rejected over Koromilas, Li and Anderson for the reasons set forth above in the 103 rejection.

However, Koromilas, Li and Anderson do not teach that the vector comprising the DNA sequence of claim 10 is a viral vector, or that the viral vector is a BK vector.

De Benedetti teaches a novel BK virus-based episomal vector for expression of foreign genes in mammalian cells. Specifically, De Benedetti teaches that the pBK shuttle vector is based on the SV40 and the human papova virus BK (see p. 1925, first column). De Benedetti also indicates that pBK is maintained in a episomal form in several human cell lines, resembling productive infection of the virus and pBK replicates at high copy number which can be varied by changing the G418 concentration in the culture medium (see p. 1925, first column).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the pBK shuttle vector taught by De Benedetti such that pBK comprised the DNA sequence suggested by Koromilas, Li and Anderson as mentioned above, with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to make a pBK vector which is capable of expressing the DNA sequence suggested by Koromilas, Li and Anderson in cells in order to make a shuttle vector capable of expressing the DNA sequence of claim 10 (suggested by Koromilas, Li and Anderson) in mammalian cells wherein the DNA sequence remains episomal and stable over long periods of time.

20. Claims 10, 22, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koromilas et al. (EMBO 1992, cited in IDS) in view of Li B.D. et al. (Cancer 1997, cited in IDS) and Anderson L.M. et al. (Gene Therapy 1999, cited in IDS), and further in view of De Benedetti et al. (Nucleic Acids Research, 1991; 8:1924-1931, cited in IDS).

It is noted that claim 27 is interpreted as the pharmaceutical composition of claim 26, and claim 26 is interpreted as the vector of claim 22, for the reasons mentioned in the 112 second paragraph rejection.

Claims 10 and 22 are rejected over Koromilas, Li and Anderson for the reasons set forth above in the 103 rejection.

However, Koromilas, Li and Anderson do not teach a pharmaceutical composition comprising the vector comprising the DNA sequence of claim 10 (suggested by Koromilas, Li and Anderson) and a liposome complex carrier.

GIBCO/BRL (1993-1994 catalogue) teaches a liposome complex carrier, known as Lipofectin reagent (see p. 9-19) that is suitable for transfecting nucleic acids into tissue culture cells. Specifically, It is indicated that Lipofectin reagent comprises a cationic lipid (DOTMA) and a neutral lipid (DOPE) which forms a liposome complex with nucleic acids. The liposome-nucleic acid complex fuses with plasma membranes and transfers the nucleic acid into the cells. It is also indicated that Lipofectin is 5- to 100-fold more efficient than calcium phosphate or DEAE-dextran transfection methods.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to take the vector comprising the DNA sequence of claim 10 (suggested by Koromilas, Li and Anderson) and combine it with the Lipofectin reagent (taught by GIBCO/BRL catalogue) in order to transfect the vector into cultured cells, with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to make the composition comprising the vector is capable of expressing the DNA sequence of claim 10 (suggested by Koromilas, Li and Anderson) and the liposome complex carrier (taught by GIBCO/BRL catalogue) in order to more efficiently transfect the vector into cells in order to express the toxin in a higher number of cells which overexpress eIF4E.

Response to Amendment/Arguments

The previous rejection of claims under 35 USC 112(2) is withdrawn in view of the amendments.

The previous rejection of claims under 35 USC 112(1) is withdrawn in view of the amendments and/or persuasive arguments.

The previous rejection under 35 USC 102(a) is withdrawn in view of the Declaration under 37 CFR 1.132 filed 10/30/02.

The previous rejection under 35 USC 103 is withdrawn in view of the amendment and/or arguments.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVE T. NGUYEN
PRIMARY EXAMINER

J. Eric Angell
January 12, 2003